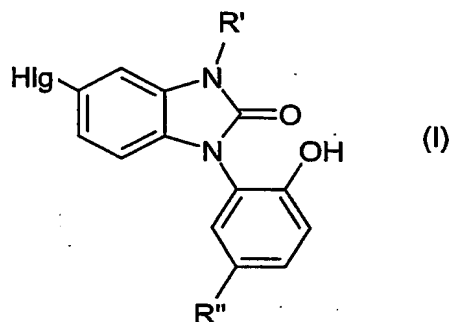


CLAIMS

1. A 1,5-disubstituted benzimidazol-2-one derivative having the general Formula I



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wherein

R' represents hydrogen or alkyl;

R'' represents halogen or trihalogenmethyl; and

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Hlg represents halogen;

provided, however, that

if Hlg is F, then R'' is not Cl.

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2. The benzimidazol-2-one derivative of claim 1, wherein Hlg represents Cl or Br.

3. The benzimidazol-2-one derivative of either of claims 1-2, wherein R' represents hydrogen or methyl.

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4. The benzimidazol-2-one derivative of any of claims 1-3, wherein R'' represents halogen or CF₃.

5. The benzimidazol-2-one derivative of claim 4, wherein R'' represents Cl or CF₃.

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6. The benzimidazol-2-one derivative of any of claims 1-5, which is 1-(5-chloro-2-hydroxyphenyl)-5-chloro-1,3-dihydro-2H-benzimidazo-2-one; or 1-(5-trifluoromethyl-2-hydroxyphenyl)-5-chloro-1,3-dihydro-2H-benzimidazo-2-one; or a pharmaceutically-acceptable salt thereof.

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7. A pharmaceutical composition comprising a therapeutically effective amount of the benzimidazol-2-one derivative of claims 1-6, or a pharmaceutically-acceptable addition salt thereof, together with at least one pharmaceutically-acceptable carrier or diluent.
- 5 8. The pharmaceutical composition of claim 7, which composition comprises a further therapeutic agent.
9. The use of a benzimidazol-2-one derivative according to any of claims 1-6, or a
10 pharmaceutically-acceptable addition salt thereof, for the manufacture of a medicament for the treatment, prevention or alleviation of a disease or a disorder or a condition of a mammal, including a human, which disease, disorder or condition is responsive to modulation of BK_{Ca} channels.
- 15 10. The use according to claim 9, wherein the disease, disorder or condition is an obstructive or inflammatory airway disease.
11. The use according to claim 10, wherein the obstructive or inflammatory airway
20 disease is an airway hyperreactivity, a pneumoconiosis such as aluminosis, anthracosis, asbestosis, chalicosis, ptilosis, siderosis, silicosis, tabacosis and byssinosis, a chronic obstructive pulmonary disease (COPD), bronchitis, exacerbation of airways hyperreactivity or cystic fibrosis.
12. The use according to claim 9, wherein the disease, disorder or condition is a
25 cardiovascular disease, in particular atherosclerosis, ischemia/reperfusion, hypertension, restenosis, arterial inflammation, myocardial ischaemia and ischaemic heart disease.
13. The use of a benzimidazol-2-one derivative according to any of claims 1-6, or a
30 pharmaceutically-acceptable addition salt thereof, for the manufacture of a medicament useful for increasing the blood-brain barrier permeability.
14. The use according to claim 13, for the manufacture of a medicament useful for
35 co-administration of a therapeutic agent.
15. The use according to claim 14, wherein the therapeutic agent is an antineoplastic agent, a chemotherapeutic agent, a cytotoxic agent, a DNA expression vector, a protein, an oligonucleotide, a nucleotide analog, an antimicrobial agent, an interferon, a cytokine, a cytokine agonist, a cytokine antagonist, an immunotoxin,

an immunosuppressant, a boron compound, a monoclonal antibody, an adrenergic agent, an anticonvulsant, an ischemia-protective agent, an anti-trauma agent, an anticancer chemotherapeutic agent or a diagnostic agent.

- 5 16. The use according to claim 15, wherein the DNA expression vector is a viral vector, preferably an adenovirus-derived vector or herpes simplex virus-derived vector.
- 10 17. The use according to claim 15, wherein the diagnostic agent is an imaging or contrast agent, preferably a radioactively labelled substance, a gallium-labelled substance, or a contrast agent selected from the group consisting of ferrous magnetic, fluorescent, luminescent, and iodinated contrast agents.
- 15 18. A kit-of-parts useful for enhancing the delivery of a medicament to the brain, which kit comprises:
A benzimidazol-2-one derivative of claims 1-6;
A therapeutic agent; and
Instructions for using the 1,5-disubstituted benzimidazol-2-one derivative for enhancing delivery of the therapeutic agent to the brain.
- 20 19. A method of treatment, prevention or alleviation of a disease or a disorder or a condition of a mammal, including a human, which disease, disorder or condition is responsive to modulation of BK_{Ca} channels, which method comprises the step of administering to such a living animal body in need thereof, a therapeutically effective amount of a benzimidazol-2-one derivative according to any of claims 1-6, or a pharmaceutically-acceptable salt thereof.
- 25 20. The method of claim 19, wherein the disease, disorder or condition is of an obstructive or inflammatory airway disease.
- 30 21. The method of claim 19, wherein the disease, disorder or condition is a cardiovascular disease.
- 35 22. A method of increasing the blood-brain barrier permeability in a living animal body, including a human, which method comprises the step of administering to such a living animal body in need thereof, a therapeutically effective amount of a benzimidazol-2-one derivative according to any of claims 1-6, or a pharmaceutically-acceptable salt thereof.

23. The method according to claim 22, which method comprises co-administration of a therapeutic agent.